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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LONG, SCOTT	
ART UNIT	PAPER NUMBER
1633	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/584,180	SHORTMAN ET AL.	
	Examiner	Art Unit	
	SCOTT LONG	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7-10 and 13-30* is/are pending in the application.

4a) Of the above claim(s) *13-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7-10 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/15/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner acknowledges receipt of Applicant's Remarks and Claim amendments, filed on 15 March 2010.

Claim Status

Claims 1, 7-10 and 13-30 are pending. Claim 30 is newly added. Claims 2-6 and 11-12 are cancelled. Claim 1 is amended. Claims 28-29 are withdrawn by the applicant. Claims 13-27 are withdrawn from further consideration by the Examiner, pursuant to 37 CFR 1.142(b), as being drawn to non-elected inventions, there being no allowable generic or linking claim. Claims 1, 7-10 and 30 are under current examination.

Priority

This application claims benefit as a 371 of PCT/AU04/01840 (filed 12/23/2004) which claims priority from Foreign Application, AUSTRALIA 2003907195 (filed 12/24/2003). The instant application has been granted the benefit date, 24 December 2003, from the Foreign Application, AUSTRALIA 2003907195

Information Disclosure Statement

The Information Disclosure Statements (IDS) filed on 15 March 2010 consisting of 1 sheet is in compliance with 37 CFR 1.97. Accordingly, examiner has considered the Information Disclosure Statements.

RESPONSE TO ARGUMENTS

35 USC § 103

The rejection of claims 1, 3 and 5-10 under 35 U.S.C. 103(a) as being unpatentable over Morin et al. (Clinical & Experimental Immunology. 134(3): 388-395; published online 24 Nov 2003) withdrawn in response to the applicants arguments and/or claim amendments.

The applicant's claim amendments have been fully considered and are persuasive.

The applicant has amended the instant claims to recite: "wherein Flt-3L is administered to said subject as the sole active component." The specification does not use the word, "component." Without the specification's guidance regarding the meaning of "active component" or "sole active component," the examiner looks to the specification to find appropriate teachings for interpreting this new claim language. The examiner is guided by the specification's teachings regarding the term "agent" to interpret the word, "component," as meaning "a therapeutic molecule" or "compound" (page 11, lines 8-10). The examiner is further guided by the specification's teachings regarding the term "active ingredient" to interpret the phrase, "active component," as being exemplified by "Flt-3L" (page 11, lines 10-12). The teachings of the specification seem to provide for interpreting the new claim language as describing Flt-3L as being the sole active ingredient, or as Flt-3L as being the sole active agent, or as Flt-3 as being the sole active compound/molecule. Further, the specification indicates that

cytokines are active agents. Morin et al. teach administration of Flt-3L, with GM-CSF and IL-6 to spleen cells to produce Dendritic cells which are transferred into non-obese diabetic mice. Morin does not teach or suggest that Flt-3L alone is sufficient to affect the phenotype of diabetic mice. Therefore, the examiner finds the applicant's claim amendments sufficient to overcome the rejection over Morin.

The examiner does not view the claim amendments as new matter because the teachings of Example 2 found in the specification at page 37.

Therefore, the examiner hereby withdraws the rejection of claims 1, 3 and 5-10 under 35 U.S.C. 103(a) as being unpatentable over Morin et al.

NEW GROUNDS OF REJECTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 7-10 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maraskovsky et al. (*J. Exp. Med.* 1996; 184: 1953-1962) in view of Morel et al. (*Clin. Exp. Immunol.* Published online 23 June 2003; 133(1): 1-10).

Claim 1 is directed to a method for delaying onset of diabetes in a subject said method comprising administering to said subject Flt-3L [Flt-3 Ligand], wherein Flt-3L is administered to said subject as the sole active component in an amount effective to increase a sub-type of non-activated, immature and tolerogenic DC selected from Plasmacytoid DC, $CD8^+$ DC or their equivalents thereby inducing or maintaining immune tolerance in said subject which delays onset of diabetes.

Maraskovsky et al. teach "in vivo administration of Flt3L results in a dramatic numerical increase of DC in multiple tissues in mice" and further indicate that a subpopulation of these dendritic cells expresses CD8α (page 1959, Discussion; Fig. 2B, population E). Maraskovsky et al. further teach dendritic cells induce immune tolerance and is promising for immunotherapy (page 1953, col.2, last 4 lines).

Maraskovsky et al. do not teach the relevance of an increased subpopulation of $CD8^+$ dendritic cells to inducing immune tolerance for delaying the onset of diabetes.

However, Morel et al. teach therapeutic effect of distinct DC subsets on autoimmune disease (Table 2), including CD8α+ dendritic cells prevent diabetes in NOD mice (Table 2). Additionally, Morel et al. teach immune tolerance is induced in mice by CD8α+ dendritic cells (page 2, col.1., lines 23-25). Furthermore, Morel suggest that this occurs in animal models of diabetes and in humans (page 5, Dendritic cells as therapeutic agents in autoimmune disease). Morel et al. also teach that increased numbers of DC cells were related to increased levels of Flt-3L (page 4, col.2, Role of Dendritic cells).

Claim 7 is directed to the method of claim 1 wherein the subject is a human, non-human primate, livestock animal, laboratory test animal, a companion animal, a captured wild animal or an avian species. Morel suggest that this mechanism occurs in animal models of diabetes and in humans (page 5, Dendritic cells as therapeutic agents in autoimmune disease).

Claim 8 is directed to the method of claim 7, wherein the subject is a human. Morel suggest that this mechanism occurs in humans (page 5, Dendritic cells as therapeutic agents in autoimmune disease).

Claim 9 is directed to the method of claim 1, wherein the Flt-3L is derived from the same species to which it is administered. The embodiment of Maraskovsky teach using Chinese hamster ovary cell (CHO)-derived Flt3L injected into mice (page 1954). However, to a skilled artisan, it is obvious to use human Flt-3L to treat humans.

Administration of recombinant human proteins to human subjects for the treatment of disease is well known and practiced among skilled artisans.

Claim 10 is directed to the method of claim 1, wherein the Flt-3L is derived from a different species to which it is administered. Maraskovsky teach using Chinese hamster ovary cell (CHO)-derived Flt3L injected into mice (page 1954).

Claim 30 is directed to the method of claim 1, wherein said subject is predisposed to developing diabetes. The NOD mouse of Morel is a model of autoimmune diabetes.

Morel et al. does not teach administering Flt-3L to the NOD mice to delay onset of diabetes.

It would have been obvious to the person of ordinary skill in the art at the time of the invention was made to administer Flt-3L to a subject to delay onset of diabetes.

The person of ordinary skill in the art would have been motivated to administer Flt-3L to a subject to delay onset of diabetes. Maraskovsky teach injection of Flt-3L into mice increases the population of CD8+ dendritic cells. Morel et al. teach the relevance of an increased subpopulation of $CD8^+$ dendritic cells to inducing immune tolerance for delaying the onset of diabetes. Therefore, a skilled artisan would conclude one could delay the onset of diabetes by inducing immune tolerance through increasing a subpopulation of $CD8^+$ dendritic cells by administering Flt-3L to subjects predisposed to diabetes. The nexus between the arts is the increase in CD8+ dendritic cells. Once a skilled artisan is aware of the need to increase the number of CD8+ dendritic cells in order to induce immune tolerance which delays the onset of diabetes, a skilled artisan

would be guided by Maraskovsky to treat the subject by administering Flt-3L, which has been proven to increase the population of CD8+ dendritic cells.

An artisan would have expected success, because Flt-3L has been shown to mature a population of CD8+ dendritic cells and CD8+ dendritic cells have been shown to be capable of delaying onset of diabetes in a diabetic mouse model.

Therefore the method as taught by Maraskovsky et al. in view of Morin et al would have been *prima facie* obvious over the method of the instant application.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claims are allowed.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Scott Long/
Patent Examiner, Art Unit 1633